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Intermediate-Term Outcome After Pulmonary Balloon Valvuloplasty: Comparison With a Matched Surgical Control Group

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To assess late (4 to 5 years) gradient reduction after pulmonary balloon valvuloplasty in childhood, and to compare the effectiveness of valvuloplasty with that of surgical valvotomy, 20 valvuloplasty-treated children and their age- and gradient-matched surgical control patients underwent prospective, noninvasive evaluation. The average age at intervention was 4.3 ± 1 years for the valvuloplasty group versus 4.7 ± 0.8 years for the surgical control group (p = NS). Before intervention the peak systolic pulmonary stenosis gradient was 76 ± 5 and 74 ± 4.4 mm Hg for the valvuloplasty and surgery groups, respectively (p = NS).

Late evaluation consisted of clinical examination, two-dimensional echocardiogram and Doppler study, 24-hour Holter monitoring, 12-lead electrocardiogram, exercise treadmill study and chest radiograph performed an average of 5.3 ± 0.3 years after valvuloplasty and 11.7 ± 0.5 years after surgery (p < 0.01). The patients treated with balloon valvuloplasty had no evidence of restenosis; the residual pulmonary stenosis gradient at follow-up was 24 ± 2.7 mm Hg (range 8 to 48) versus 35 ± 3.6 mm Hg (range 19 to 70) immediately after valvuloplasty (p = NS).

Comparison of the late residual gradients between treatment groups showed no *hemodynamically* significant difference (24 ± 2.7 versus 16 ± 1.5 mm Hg, balloon versus surgery; p < 0.01). However, there was a significant difference in the degree and severity of pulmonary valve insufficiency and ventricular ectopic activity between groups. In the balloon valvuloplasty group 11 patients had no pulmonary insufficiency, and the remaining 9 had mild insufficiency. In the surgery group 9 had mild and 9 had moderate valve insufficiency (p < 0.01). Ventricular ectopic activity was absent in 19 of the balloon valvuloplasty group, and the remaining patient had Lown grade 1 ventricular ectopic activity. In contrast, 6 children in the surgery group had complex ventricular arrhythmia (p < 0.01).

In summary, compared with surgical valvotomy, balloon valvuloplasty for isolated valvular pulmonary stenosis provides nearly equivalent long-term gradient relief with less valvular insufficiency and less late ventricular ectopic activity.

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Over the past decade balloon valvuloplasty has become an accepted therapeutic alternative to surgical valvotomy for children with valvular pulmonary stenosis. The first transcatheter intervention in a child with valvular pulmonary stenosis was reported by Semb et al. (1) in 1979. Subsequently, Kan et al. (2) reported on the first series of percutaneous balloon valvuloplasty for congenital pulmonary valve stenosis in 1982. An immediate and substantial reduction in the right ventricular outflow gradient was demonstrated in all patients. Since then, valvuloplasty has been shown to be acutely effective in reducing the obstruction to right ventricular outflow in children with valvular pulmonary stenosis (3–12). Though short-term follow-up studies have shown persistent gradient relief, systematic longer-term follow-up studies are lacking.

The purpose of the current study was to prospectively and systematically assess the intermediate-term (≥4 years) gradient reduction after balloon valvuloplasty for isolated valvular pulmonary stenosis in childhood. In addition, the residual outflow gradient and degree of restenosis were compared with those achieved by surgical valvotomy. Finally, comparisons were drawn between balloon valvuloplasty and surgery for the presence and degree of pulmonary valve insufficiency, ventricular arrhythmias and aerobic work capacity at late follow-up.

Methods

Study group. The valvuloplasty-treated group consisted of those children who underwent balloon valvuloplasty for isolated valvular pulmonary stenosis at C.S. Mott Children's Hospital between 1982 and 1986. Patients with a dysplastic pulmonary valve, pulmonary valve anulus hypoplasia and

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complex right ventricular outflow obstruction were excluded from the study. During this time interval, all children presenting to our institution with isolated valvular pulmonary stenosis underwent percutaneous pulmonary balloon valvuloplasty. Of the 24 children treated with balloon valvuloplasty during this interval, 3 were lost to follow-up and 1 refused participation in the study. Thus, the study group consisted of the remaining 20 children. No child treated with balloon valvuloplasty required subsequent intervention.

Control group. Because of the acceptance of pulmonary balloon valvuloplasty at our institution since 1982, a chronologically concurrent surgical control group was not available for comparison. The surgical control group, therefore, consisted of 20 children treated with surgical valvotomy for isolated valvular pulmonary stenosis between 1978 and 1982. These patients were selected to match the valvuloplasty group closely for age and valve gradient at the time of intervention.

Follow-up evaluation. Follow-up study consisted of clinical examination of each patient by two clinicians. Additionally, all patients underwent a standard 12-lead electrocardiogram (ECG), posteroanterior and lateral chest radiographs, two-dimensional echocardiogram with continuous wave and color flow Doppler examination, 24-h two-channel Holter ECG monitor recording and a graded exercise treadmill test with breath by breath gas analysis. Informed consent was obtained for the follow-up study, which was approved by the Medical Center Institutional Review Board on January 12, 1989.

The residual pulmonary stenosis gradient was estimated from continuous wave Doppler peak instantaneous gradients obtained from several echocardiographic windows. The highest gradient calculated was reported as the residual pulmonary stenosis gradient. Pulmonary insufficiency, for the purposes of the current study, was quantitated by using a combination of clinical and echocardiographic findings as follows. Pulmonary insufficiency was considered to be absent in patients who had no diastolic murmur on clinical examination and no right ventricular volume overload by two-dimensional echocardiogram; mild pulmonary insufficiency was characterized by a grade 1–2/4 diastolic murmur without right ventricular volume overload on echocardiogram; moderate pulmonary insufficiency was characterized by a grade 2–3/4 diastolic murmur together with right ventricular volume overload and flattened or paradoxic septal motion on echocardiogram.

Ventricular ectopic activity documented by 24-h Holter monitor recordings was quantitated using the Lown criteria (13). Maximal oxygen consumption, anaerobic threshold, heart rate and blood pressure response, ischemic changes and presence of arrhythmia were assessed during graded treadmill exercise study. Right ventricular forces were quantitated from the rest ECG by measurement of the R wave voltage in leads V_1 and V_4R. The cardiothoracic ratio was measured on the chest radiograph in all children.

Table 1. Pertinent Clinical and Hemodynamic Data in the Balloon Valvuloplasty and Surgical Control Groups

	Valvuloplasty Group (n = 20)	Surgery Group (n = 20)	p Value
Age at intervention (yr)	4.3 ± 1	4.7 ± 0.8	NS*
Initial PS gradient (mm Hg)	76 ± 5	74 ± 4.4	NS*
Follow-up duration (yr)	5.3 ± 0.3	11.7 ± 0.5	<0.01
Residual PS gradient (mm Hg)	24 ± 2.7	16 ± 1.5	<0.01
Pulmonary insufficiency			<0.01
None	11	2	
Mild	9	9	
Moderate	0	9	
Ventricular ectopic activity (Lown grade)			<0.01
None	19	6	
Grade 1	1	8	
Grade 2	0	1	
Grade 3	0	2	
Grade 4	0	3	

*Not significant at $p < 0.05$. PS = pulmonary stenosis.

Data analysis. Continuous data are presented as mean value ± 1 SE. Serial pulmonary stenosis gradients immediately before treatment, immediately after treatment and at late follow-up evaluation were compared within the valvuloplasty and surgical valvotomy groups by using repeated measures analysis of variance. Comparisons between the two groups were performed by using a two-tailed, paired Student *t* test. The prevalence of late ventricular arrhythmias, the degree of pulmonary valve insufficiency and exercise capacity were compared between patient groups by using an unpaired Student *t* test to compare continuous data and a contingency table analysis to compare categoric data. A p value < 0.05 was required for evidence of a statistically significant difference.

Results

Study group. The average age at intervention for the balloon valvuloplasty children was 4.3 ± 1 years (range 0.7 to 17.5) (Table 1), and the pressure gradient to right ventricular outflow averaged 76 ± 5 mm Hg (42 to 120). A single-balloon valvuloplasty procedure was performed in 18 children and a double-balloon procedure in 2 children. The ratio of anulus to balloon diameter was 1.2 ± 0.05 (range 0.8 to 1.6) in those patients treated with a single balloon and 1.2 and 1, respectively, in the two children treated with a double-balloon technique (14,15).

The pulmonary stenosis gradient was reduced immediately after valvuloplasty from 76 ± 5 mm Hg (range 42 to 120) to 35 ± 3.2 mm Hg (range 19 to 57) ($p < 0.01$) without a significant change in cardiac index or heart rate after balloon valvuloplasty. This difference represents a 54% immediate reduction in the gradient to right ventricular outflow. Similarly, the right ventricular systolic pressure

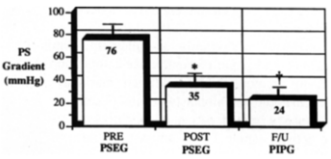

Figure 1. Serial pulmonary stenosis (PS) gradients in the 20 patients in the valvuloplasty group immediately before (PRE) and immediately after (POST) valvuloplasty and at an average follow-up duration of 5.4 ± 0.3 years (F/U). *$p < 0.01$ versus value immediately before valvuloplasty. †$p < 0.01$ versus value immediately after valvuloplasty. PIPG = peak instantaneous pressure gradient; PSEG = peak systolic ejection gradient.

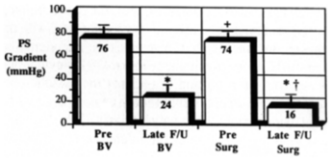

Figure 2. Comparison of the pulmonary stenosis (PS) gradient before intervention (Pre) to that at late follow-up (Late F/U) for the 20 children treated with balloon valvuloplasty (BV) and the 20 treated with surgical valvotomy (Surg). *$p < 0.01$ versus value before valvuloplasty or surgery. †$p < 0.01$ versus value at late follow-up after valvuloplasty. +p = NS versus value before valvuloplasty.

was reduced immediately after valvuloplasty from 96 ± 5 to 56 ± 4 mm Hg ($p < 0.01$).

Surgical control group. All 20 surgically treated patients underwent an open surgical valvotomy. Three children also underwent suture closure of a patent foramen ovale. None had a transannular patch, ventriculotomy or infundibular muscle resection. The mean age at operation (Table 1) was 4.7 ± 0.8 years (range 0.3 to 12.5), and the pulmonary stenosis gradient before operation was 74 ± 4.4 mm Hg (range 55 to 120). These 20 patients were individually matched for age to within 0.3 ± 0.6 year with the corresponding valvuloplasty patient (p = NS), and the peak pulmonary stenosis gradient for each patient pair was matched to within 2.5 ± 2.5 mm Hg (p = NS). Thus, the two patient groups were nearly identical with respect to age and pulmonary stenosis gradient at the time of intervention. There was also no difference between groups in right ventricular systolic pressure, aortic systolic pressure, heart rate or cardiac index before intervention.

Follow-up data. The pulmonary outflow gradient at follow-up (5.3 ± 0.3 years [range 4 to 8]) remained significantly reduced in the balloon valvuloplasty group. The Doppler *peak instantaneous* pulmonary stenosis gradient at follow-up was 24 ± 2.7 mm Hg (range 8 to 48) which was 10 mm Hg lower than the *peak to peak* systolic gradient measured at cardiac catheterization immediately after valvuloplasty ($p < 0.01$). Furthermore, the gradient at follow-up evaluation remained greatly reduced in comparison with that before intervention (Fig. 1). The residual pulmonary stenosis gradient for the surgical group averaged 16 ± 1.5 mm Hg at follow-up, significantly lower than the residual gradient documented in the balloon valvuloplasty group ($p < 0.01$) (Fig. 2).

At follow-up, patients in the balloon valvuloplasty group demonstrated no more than mild valvular insufficiency. Eleven of these 20 children had no pulmonary insufficiency, and the remaining 9 had mild insufficiency. The surgically treated patients, demonstrated predominantly mild to moderate pulmonary valve insufficiency at follow-up; only 2 had no pulmonary regurgitation. Nine children had mild and 9 had moderate valvular insufficiency ($p < 0.01$) (Table 1).

Ventricular ectopic activity was absent in all but one patient in the valvuloplasty group, who had rare uniform ventricular premature complexes (Lown grade 1) (Table 1). Thus 19 (95%) of 20 patients in this group had no ventricular arrhythmia at follow-up. In contrast, only 6 of the 20 surgically treated children had no ventricular ectopic activity and 6 (30%) had complex ectopic activity (≥grade 2) documented on Holter evaluation. Of these six patients, one had grade 2 and two had grade 3 ventricular ectopic activity (multiform ventricular premature complexes); three demonstrated grade 4 ventricular arrhythmia (couplets in one patient and nonsustained ventricular tachycardia in two patients).

Follow-up studies that demonstrated no difference between the balloon valvuloplasty and surgical groups included maximal oxygen consumption and duration of exercise on graded exercise treadmill study, right ventricular forces, QRS axis and QRS duration on the resting 12-lead ECG and cardiothoracic ratio on chest radiography. Because the chronologic time of treatment differed between groups, follow-up durations were different, averaging 5.3 ± 0.3 years (range 4 to 7.8) for the balloon valvuloplasty group and 11.7 ± 0.5 years (range 9.1 to 15.8) for the surgical control group ($p < 0.01$) (Table 1).

Discussion

Results of balloon valvuloplasty. Traditionally, patients with isolated valvular pulmonary stenosis have undergone surgical valvotomy to relieve the obstruction to right ventricular outflow. Over the past 7 to 8 years, however, balloon valvuloplasty has gained acceptance as an alternative to surgery for isolated valvular pulmonary stenosis in childhood and adolescence. In a prospective, systematic fashion, the current study has documented persistent gradient relief at follow-up 4 to 7.8 years after balloon valvuloplasty in a representative pediatric population with isolated valvular

pulmonary stenosis. Comparison of the peak pulmonary stenosis gradient immediately after valvuloplasty with that at follow-up documents that restenosis is uncommon after successful balloon valvuloplasty for *isolated* valvular pulmonary stenosis. In a portion of patients the systolic outflow gradient actually decreased at follow-up compared with that present immediately after valvuloplasty (Fig. 1). This decrease reflects resolution of the infundibular component to outflow obstruction, as previously suggested by Thapar and Rao (11). Unlike data recently reported by McCrindle and Kan (16), our data do not suggest that the late residual gradient is greater when balloon valvuloplasty is performed in children <2 years of age (<2 years 22.9 ± 3.5 mm Hg, >2 years 25.4 ± 4 mm Hg; p = 0.67).

Comparison with surgical results. No previous study has directly compared the late outcome of balloon valvuloplasty with that of surgery in patients with valvular pulmonary stenosis. The present study does so, and in two groups nearly identical with respect to age and stenosis gradient at intervention. Because of differences in the time of intervention, the two groups differ with respect to follow-up duration. This difference should not bias the comparison of residual pulmonary stenosis gradients between groups, however, because the natural history study reported by Nugent et al. (17) has shown that residual right ventricular outflow obstruction rarely progresses over time after surgical valvotomy. The current study, then, documents that balloon valvuloplasty provides persistent gradient relief that we believe is clinically equivalent to that obtained with surgical valvotomy. Although the average residual pulmonary stenosis gradient after valvotomy was statistically lower than that after valvuloplasty (16 ± 1.5 versus 24 ± 2.7 mm Hg), an 8 mm Hg difference is unlikely to be hemodynamically or clinically significant. Furthermore, these late follow-up data were obtained in the earliest cohort of patients treated with balloon valvuloplasty at our institution and therefore represent our early "learning curve." The highest residual pulmonary stenosis gradients were noted in three patients who underwent pulmonary valve dilation performed with a balloon that we would currently regard as undersized (balloon/annulus ratio 0.8 to 0.9). When these patients were excluded from the comparison, the residual pulmonary stenosis gradient at follow-up did not differ statistically between the valvuloplasty and surgical valvotomy groups.

Pulmonary insufficiency at follow-up. In this study the prevalence of pulmonary valve insufficiency at follow-up was greater after surgical valvotomy than after balloon valvuloplasty. Pulmonary insufficiency, quantitated with clinical and echocardiographic criteria, was more common and more severe in the surgical group than in the balloon valvuloplasty group. Although an equivalent follow-up duration is necessary to definitively compare the prevalence of late complications between groups, the difference in prevalence of moderate pulmonary insufficiency is dramatic (Table 1). No patient in the valvuloplasty group demonstrated more than mild valve insufficiency, whereas nearly half of the surgically treated patients had moderate pulmonary insufficiency.

Ventricular arrhythmia at follow-up. Similarly, the prevalence and grade of ventricular ectopic activity in the surgically treated children differed markedly from that in the balloon valvuloplasty group (Table 1). Only one valvuloplasty-treated patient demonstrated ventricular ectopic activity (grade 1). In contrast, in the surgical group, multiform ventricular extrasystoles were demonstrated in two children, couplets in one child and nonsustained ventricular tachycardia in two children. In one of these children chest pain and palpitation were noted during episodes of ventricular tachycardia. Duration of follow-up and hemodynamic status have been shown (18) to relate to the development of late ventricular arrhythmias after repair of tetralogy of Fallot. The marked increase in the prevalence and complexity of late ventricular arrhythmia in the surgical group may therefore relate to the longer follow-up duration or to the greater degree of pulmonary insufficiency present in these patients.

Strengths and limitations. A strength of the present study is its inclusion of a relatively large proportion of the children who were treated with balloon pulmonary valvuloplasty at our institution with a follow-up period of ≥4 years. In all, 20 of 24 children with isolated valvular pulmonary stenosis who underwent balloon pulmonary valvuloplasty between 1982 and 1986 at our institution participated in the follow-up study. The study is limited by the differences in time period of treatment in the valvuloplasty and surgical groups. Data obtained 4 to 8 years after valvuloplasty may not be comparable with data obtained 9 to 15 years after surgical valvotomy. It is unlikely that these differences should pose a significant limitation to the conclusions drawn from the current data regarding residual outflow obstruction. The natural history study reported by Nugent et al. (17) has shown that a residual pulmonary stenosis gradient rarely progresses over time after surgical pulmonary valvotomy. A longer follow-up duration will be necessary to determine whether the valvuloplasty-treated children will eventually develop the degree of pulmonary valve insufficiency or ventricular ectopic activity documented in the surgical control group.

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